REMARKS

Claims 2, 59-71, and 83-84 have been canceled without prejudice. Claims 1, 20, 43, 85, and 87 have been amended. Support for the amendments can be found throughout the specification (e.g., page 17, lines 5-9; page 19, line 32; page 20, lines 1-7; and Figures 1B, 3A, and 5) and original claims (e.g., claims 3-7). No new matter has been introduced and no new issues have been raised. These amendments have been made solely to expedite allowance of claims. Applicants reserve the right to pursue claims of similar or differing scope in the future.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Election/Restrictions

The Examiner has acknowledged Applicants' election with traverse of the species (SEQ ID NO: 7) in the Response filed on July 23, 2007. The Examiner has withdrawn claims 32 and 85-87 as allegedly being drawn to nonelected subject matter, there being no allowable generic or linking claim. See Office Action, page 2, second paragraph.

Applicants respectfully traverse the Examiner's withdrawal of claims 32 and 86. Claims 32 and 86 relate to SEQ ID NO: 5 (a fusion protein of human RAGE-LBE and an Fc domain), which is clearly a species of the fusion protein of claim 1. As evidenced in the specification and the pending claims, an extracellular portion of SEQ ID NO: 7 constitutes the RAGE-LBE of the claimed fusion protein. Further, Applicants remind the Examiner that independent claim 1 is a generic and linking claim for the elected and non-elected sequence species. As such, restrictions imposed on species encompassed by generic claims must be withdrawn upon indication of an allowable generic claim (MPEP 809).

Claim Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-2, 8-31, and 42-44 and 27-29 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Specifically, the Office Action asserts that "the claims are genus claims because the specification (and claims) do not set forth the structure of the multitude of RAGE-LBE's, TNF-α inhibitors, dimerizing polypeptides including amphiphilic polypeptides, purification polypeptides, stabilizing polypeptides, and targeting polypeptides that are encompassed by the claims." See Office Action, the paragraph bridging pages 4 and 5.

Applicants reiterate the arguments already made of record and submit that the specification sufficiently describes the claimed invention. Nevertheless, solely to expedite prosecution of the application, claims 1, 20, and 43 have been amended such that they are directed to a human RAGE-LBE fusion protein. Claims 1, 20, and 43 as amended recite that the RAGE-LBE comprises at least 118 amino acids and is at least 95% identical to amino acid residues 1 through 118 of SEQ ID NO: 7 (human RAGE. Support for the amendments can be found throughout the specification (e.g., page 12, lines 14-18; page 17, lines 5-9; page 19, line 32; page 20, lines 1-7; and Figures 1B, 3A, and 5) and original claims (e.g., claims 3-7). Further, the term "RAGE-LBE" is functionally defined in the specification to include "any extracellular portion of a transmembrane RAGE polypeptide (e.g., soluble RAGE) and fragments thereof that *retain the ability to bind a RAGE ligand*" (page 12, lines 10-13). Accordingly, the genus directed to the RAGE-LBE as recited in amended claims 2, 20, and 43 is structurally and functionally defined.

In addition, Applicants have amended claims 85 and 87 which relate to a mouse RAGE-LBE (SEQ ID NO: 2) as shown in Figure 1B. Since the mouse RAGE-LBE is about 77% identical to human RAGE-LBE, Applicants have converted claims 85 and 87 into independent claims. Claims 85 and 87 as amended are each directed to a fusion protein comprising a RAGE-LBE, wherein said RAGE-LBE comprises an amino acid sequence at least 95% identical to SEQ ID NO: 2. Similarly, the genus directed to the RAGE-LBE as recited in amended claims 85 and 87 is structurally and functionally defined.

In particular, the Examiner asserts that "only isolated fusion proteins comprising the amino acid sequence set forth in residues 1-344 of SEQ ID NO: 7 or comprising the amino acid sequence set forth in SEQ ID NO: 2, but not the full breath of the claim meets the written description provision of 35 U.S.C. 112." Office Action, page 6, last paragraph.

Applicants respectfully disagree. Applicants draw the Examiner's attention to a recent PTO Board decision, which supports Applicants' position that the specification provides adequate written description for the recited genus of RAGE-LBE in the amended claims. *See Ex parte Bandman*, No. 2004-2319, (BPAI 2005). Claims 3 of the U.S. Application No. 09/915,694 ('694 application) in *Bandman*, which was representative of the subject matter on appeal, recites, *inter alia*, "an isolated polynucleotide encoding a polypeptide comprising a naturally occurring amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 1." In *Bandman*, Applicants appealed a Final rejection by the Examiner, and the Board reversed the rejections based on both the written description and enablement requirements of 35 U.S.C. § 112, first paragraph to one of the claims on appeal. Pointedly, the Board found that claims directed to a naturally occurring amino acid (or polynucleotide) sequence at least 95% identical to the disclosed amino acid (or polynucleotide) sequence were enabled and met the written description requirement, even in the absence of explicitly reciting a *functional requirement* of the claimed sequences. The Board noted that "[t]he written description requirement . . . does not require a description of the complete structure of every species within a chemical genus." *Bandman*, No. 2004-2319 at p. 3. The Board also compared the circumstances of *Bandman* with those faced by the Federal Circuit in *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316 (Fed. Cir. 2002). In *Enzo Biochem*, the Federal Circuit determined that an "[a]dequate written description may be present for a genus of nucleic acids based on their hybridization properties, 'if they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar.'" (citing *Enzo Biochem*, 296 F.3d at 1324). Thus, in *Bandman*, the Board determined that the genus of molecules defined by the claims was similarly limited, and reversed the Examiner's written description rejection.

Further, Applicants respectfully traverse the Examiner's rejections directed to the genus of TNF-α inhibitors, dimerizing polypeptides including amphiphilic polypeptides, purification polypeptides, stabilizing polypeptides, and targeting polypeptides that are encompassed by claims 20, 43, and 44. Applicants point out that where, as in this case, (1) the inventive portion of the subject matter is disclosed and (2) any additional variability within the genus arises due to additional elements that are not part of the inventor's contribution, and when the level of knowledge

and skill in the art would allow one skilled in the art to recognize that the applicant was in possession of the genus, the written description cannot be deemed defective. See Written Description Guidelines Training Materials available at http://www.uspto.gov/web/offices/pac/writtendesc.pdf (released March 1, 2000, Example 8, page 35).

One of skill in the art would know that the inventive portion of the claimed fusion proteins lies in the unique merging of technological features known in the art. As described above, the specification provides both working examples and sufficient description of the structural and functional characteristics of the genus of the claimed fusion proteins. Moreover, at the time this application was filed, TNF-α inhibitors, dimerizing polypeptides including amphiphilic polypeptides, purification polypeptides, stabilizing polypeptides, and targeting polypeptides were known and understood in the art. In accordance with the written description guidelines and the MPEP, "[i]nformation which is well known in the art need not be described in detail in the specification." Written Description Guidelines for the Examination of Patent Applications, section II, page 1105, column 3; MPEP 2163.

For the above reasons, Applicants maintain that all pending claims are supported by the specification with sufficient detail, and in light of the detailed description provided in the specification and the level of skill in the art, that Applicants were in possession of the claimed invention at the time this application was filed. Accordingly, reconsideration and withdrawal of rejection are respectfully requested.

Claim Rejection under 35 U.S.C. § 112, First Paragraph

Claims 1-2, 8-31, and 42-44 are rejected for lack of enablement. Applicants respectfully traverse these rejections to the extent it is maintained over the claims as amended.

Specifically, the Office Action asserts that "the specification, while being enabling for RAGE-LBE fusion proteins comprising the amino acid sequence set forth in residues 1-344 of SEQ ID NO: 7 or comprising the amino acid sequence set forth in SEQ ID NO: 2, does not reasonably provide enablement for RAGE-LBE fusion proteins comprising at least 70% homology with an

extracellular portion of SEQ ID NO: 7 and also comprising any TNF-α inhibitor, any dimerizing polypeptide including any amphiphilic polypeptide, any purification polypeptide, any stabilizing polypeptide, or any targeting polypeptide." Office Action, page 7, second paragraph.

Applicants respectfully disagree. As mentioned above, Applicants have amended independent claims 1 and 20 to specify the structural and functional features of the RAGE-LBE in the claimed fusion proteins. Applicants believe that such amendments render the rejection moot and the specification as filed is enabling for the full scope of the claimed invention. The specification teaches successful production of RAGE-LBE fusion proteins which retain the ability to bind to a RAGE ligand as well as therapeutic applications of these fusion proteins in diseases such as arthritis. The specification provides specific examples of RAGE-LBE fusion proteins (including mouse and human RAGE-LBE-Fc fusions) (see, e.g., Example 3 on pages 66-68; Example 5 on pages 71-72; and Example 6 on 72-73). The specification provides a representative number of examples, thereby enabling the full scope of the claims. Further, the level of skill in the art was high at the time of the filing date of the present application. In fact, the techniques involved in practicing the invention, all of which were well known in the art even before the filing date, are highly reliable and can be readily practiced by a skilled artisan.

Moreover, Applicants remind the Examiner that there is no legal requirement to disclose all species of the claimed invention to show the operativeness. The law does not impose such a formidable burden on inventors seeking patent protection. "Appellants (here, Applicants) are not required to disclose every species encompassed by their claims even in an unpredictable art" (emphasis original). *In re Angstadt*, 190 USPQ 214, 218 (CCPA 1976). Such a holding is only reasonable, since it is very difficult, if not impossible, to test and disclose all operative species in the chemical and biotechnology fields. As further pointed out by the Angstadt court "[w]ithout undue experimentation or effort or expense the combinations which do not work will readily be discovered and, of course, nobody will use them and the claims do not cover them." *Id*, at 219.

In sum, Applicants' working examples demonstrate how to make and use the RAGE-LBE fusion proteins. Therapeutic benefits of these RAGE-LBE fusion proteins are also disclosed.

Applicants contend that the pending claims are enabled throughout their scope. Applicants respectfully request that the Examiner reconsider and withdraw the enablement rejection.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 1-2, 8-31, and 42-44 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Morser et al. (US Pat. No. 5,864,018) in view of Peppel et al. (J Exp Med. 1991, 174(6):1483-9), further in view of Milne Edwards et al. (U.S. 2002/0102604) and as evidenced by Spriggs et al. (WO 94/10308). Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

According to the Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 In View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* (Federal Register Vol. 72, No. 195 at pages 57,526-57,535) (effective October 10, 2007) ("the Guidelines"), a § 103 claim rejection based on a purported teaching, suggestion or motivation to combine prior art references to arrive at the claimed invention must support a conclusion of obviousness by including: (1) a finding that there was some teaching, suggestion or motivation (TSM) to modify or combine the cited references; (2) a finding that there was a reasonable expectation of success; and (3) whatever additional findings based on the *Graham* factual inquiries may be necessary in view of the specific facts.

Applicants submit that the combination of Morser et al., Peppel et al., and Milne Edwards et al. as evidenced by Spriggs et al. fails to satisfy the criteria necessary for rendering the claimed invention obvious.

As described above, Applicants have amended independent claims 1 and 20 solely in the interests of expediting prosecution. Claims 1 and 20 as amended are directed to a fusion protein comprising a human RAGE-LBE, wherein the RAGE-LBE comprises at least 118 amino acids and is at least 95% identical to amino acid residues 1 through 118 of SEQ ID NO: 7. In addition, Applicants have amended claims 85 and 87 such that these claims are directed to a fusion protein comprising a mouse RAGE-LBE. Claims 85 and 87 as amended specify that said RAGE-LBE comprises an amino acid sequence at least 95% identical to SEQ ID NO: 2.

Morser et al. disclose fusion proteins comprising RAGE polypeptides and fragments thereof. However, Morser et al. do **not** teach or suggest the human RAGE-LBE as recited in claims 1 and 20 or the mouse RAGE-LBE as recited in claims 85 and 87. None of the other cited references (Peppel et al., Milne Edwards et al., or Spriggs et al.) bridge the gap between Morser et al. and the claimed invention. Even if Morser et al. is combined with the other cited references, the combination still fails to provide any suggestion or motivation for a skilled artisan to modify Morser's RAGE polypeptides to arrive at the claimed RAGE-LBE fusion proteins. Morser provides no teaching or suggestion that RAGE polypeptides need to be further modified to improve their suitability or efficacy for any application. Also, there is simply no common connection between these cited disclosures that would have motivated a person skilled in the art to combine these teachings to make the RAGE-LBE fusion proteins such as those claimed in the present application.

Applicants note that the Examiner has indicated that claims 3-7 and 88-92 (directed to specific sequences of RAGE-LBE) are not obvious over the cited references. Amended claims 1 and 20 are essentially drawn to the subject matter of claims 3-7 and 88-92. Thus, Applicants believe amendments to claims 1 and 20 obviate the obviousness rejection. For the same reasons, all claims depending from claim 1 or 20 are not obvious over the cited references.

Further, Applicants submit that amended claims 85 and 87 (directed to mouse RAGE-LBE fusion proteins) are not obvious over the cited references for the same reasons.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (617) 951-7000. If a fee is due, please charge our Deposit Account No. 18-1945, under Order No. **WYTH-P01-002** from which the undersigned is authorized to draw.

Dated: February 20, 2008

Respectfully submitted,

By _____

Z. Angela Guo
Registration No.: 54,144
ROPES & GRAY LLP
One International Place
Boston, Massachusetts 02110-2624
(617) 951-7000
(617) 951-7050 (Fax)
Attorneys/Agents For Applicant